# CONTENTS

## Biomarkers in Human Cancer—Part I. Predisposition and Use in Risk Assessment


**Preface** ..... 3

### Molecular, Chromosomal and Cellular Susceptibility Markers in the Multi-Stage Carcinogenesis Process in Humans

**T. Sugimura, M. Terada, J. Yokota, S. Hirohashi, and K. Wakabayashi.** Multiple genetic alterations in human carcinogenesis ..... 5

**M. W. Anderson, S. H. Reynolds, M. You, and R. M. Maronpot.** Role of proto-oncogene activation in carcinogenesis ..... 13

**H. J. Evans and J. Prosser.** Tumor-suppressor genes: cardinal factors in inherited predisposition to human cancers ..... 25

**H. Yamasaki, A. Loktionov, and L. Tomatis.** Perinatal and multigenerational effect of carcinogens: possible contribution to determination of cancer susceptibility ..... 39

**D. A. Scicchitano and P. C. Hanawalt.** Intragenomic repair heterogeneity of DNA damage ..... 45

**M. Dabholkar, L. Bradshaw, R. J. Parker, I. Gill, F. Bostick-Bruton, F. M. Muggia, and E. Reed.** Cisplatin-DNA damage and repair in peripheral blood leukocytes *in vivo* and *in vitro* ..... 53

**A. Weston, N. E. Caporaso, L. S. Perrin, H. Sugimura, S. Tamai, T. G. Krontiris, B. F. Trump, R. N. Hoover, and C. C. Harris.** Relationship of H-*ras*-1, L-*myc*, and *p53* polymorphisms with lung cancer risk and prognosis ..... 61

### Genetic Polymorphisms in Xenobiotic-Metabolizing Enzymes and Cancer Susceptibility

**F. F. Kadlubar, M. A. Butler, K. R. Kaderlik, H-C. Chou, and N. P. Lang.** Polymorphisms for aromatic amine metabolism in humans: relevance for human carcinogenesis ..... 69

**F. P. Guengerich, T. Shimada, K. D. Raney, C-H. Yun, D. J. Meyer, B. Ketterer, T. M. Harris, J. D. Groopman, and F. F. Kadlubar.** Elucidation of catalytic specificities of human cytochrome P450 and glutathione *S*-transferase enzymes and relevance to molecular epidemiology ..... 75

**F. J. Gonzalez and H. V. Gelboin.** Human cytochromes P450: evolution and cDNA-directed expression ..... 81

**B. Ketterer, J. M. Harris, G. Talaska, D. J. Meyer, S. E. Pemble, J. B. Taylor, N. P. Lang, and F. F. Kadlubar.** The human glutathione *S*-transferase supergene family, its polymorphism, and its effects on susceptibility to lung cancer ..... 87

**P. Vineis and G. Ronco.** Interindividual variation in carcinogen metabolism and bladder cancer risk .. 95

**N. E. Caporaso, P. G. Shields, M. T. Landi, G. L. Shaw, M. A. Tucker, R. Hoover, H. Sugimura, A. Weston, and C. C. Harris.** The debrisoquine metabolic phenotype and DNA-based assays: implications of misclassification for the association of lung cancer and the debrisoquine metabolic phenotype ..... 101

**C. A. D. Smith, J. E. Moss, A. C. Gough, N. K. Spurr, and C. R. Wolf.** Molecular genetic analysis of the cytochrome P450-debrisoquine hydroxylase locus and association with cancer susceptibility .... 107

**D. A. Bell, C. L. Thompson, J. Taylor, C. R. Miller, F. Perera, L. L. Hsieh, and G. W. Lucier.** Genetic monitoring of human polymorphic cancer susceptibility genes by polymerase chain reaction: application to glutathione transferase μ ..... 113

**H. Bartsch, S. Petruzzelli, S. De Flora, E. Hietanen, A.-M. Camus, M. Castegnaro, K. Alexandrov, M. Rojas, R. Saracci, and C. Giuntini.** Carcinogen metabolism in human lung tissues and the effect of tobacco smoking: results from a case–control multicenter study on lung cancer patients ..... 119

**G. Clark, A. Tritscher, D. Bell, and G. Lucier.** Integrative approach for evaluating species and interindividual differences in responsiveness to dioxins and structural analogs ..... 125

## Assessment of Carcinogen Exposure and the Use of Other Risk Markers in Populations

**F. Perera, D. Brenner, A. Jeffrey, J. Mayer, D. Tang, D. Warburton, T-L. Young, L. Wazneh, L. Latriano, G. Motykiewicz, E. Grzybowska, M. Chorazy, K. Hemminki, and R. Santella.** DNA adducts and related biomarkers in populations exposed to environmental carcinogens ..... 133

## Contributions from Molecular/Biochemical Epidemiology in Cancer Risk Assessment and Prevention

**D. W. Gaylor, F. F. Kadlubar, and F. A. Beland.** Commentary. Application of biomarkers to risk assessment ..... 139

**P. A. Schulte.** Commentary. Biomarkers in epidemiology: scientific issues and ethical implications .... 143

**R. B. Hayes.** Commentary. Biomarkers in occupational cancer epidemiology: considerations in study design ..... 149

## Critical Appraisals of Progress, Priorities, and Proper Design in Epidemiological Uses of Biomarkers

**P. H. M. Lohman, B. Morolli, F. Darroudi, A. T. Natarajan, J. A. Gossen, J. Venema, L. H. F. Mullenders, E. W. Vogel, H. Vrieling, and A. A. van Zeeland.** Contributions from molecular/biochemical approaches in epidemiology to cancer risk assessment and prevention ..... 155

**G. N. Wogan.** Molecular epidemiology in cancer risk assessment and prevention: recent progress and avenues for future research ..... 167

## Manuscripts from Presented Posters

## Molecular, Chromosomal, and Cellular Susceptibility Markers in the Multi-stage Carcinogenesis Process in Humans

**S. Anttila, H. Vainio, E. Hietanen, A.-M. Camus, C. Malaveille, G. Brun, K. Husgafvel-Pursiainen, L. Heikkilä, A. Karjalainen, and H. Bartsch.** Immunohistochemical detection of pulmonary cytochrome P450IA and metabolic activities associated with P450IA1 and P450IA2 isozymes in lung cancer patients ..... 179

**K. Husgafvel-Pursiainen, M. Ridanpää, P. Hackman, S. Anttila, A. Karjalainen, A. Onfelt, A.-L. Børrensen, and H. Vainio.** Detection of *ras* gene mutations in human lung cancer: comparison of two screening assays based on the polymerase chain reaction ..... 183

**D. Ryberg, T. Tefre, V. Skaug, L. Stangeland, S. Øvreboø A. Naalsund, A.-L. Børrensen, and A. Haugen.** Allele diversity of the H-*ras*1 variable number of tandem repeats in Norwegian lung cancer patients ..... 187

**P. G. Shields, H. Sugimura, N. E. Caporaso, S. F. Petruzzelli, E. D. Bowman, B. F. Trump, A. Weston, and C. C. Harris.** Polycyclic aromatic hydrocarbon–DNA adducts and CYP1A1 restriction fragment length polymorphism ..... 191

**M. C. Archer, W. R. Bruce, C. C. Chan, D. E. Corpet, A. Medline, L. Roncucci, D. Stamp, and X-M. Zhang.** Aberrant crypt foci and microadenoma as markers for colon cancer ..... 195

**L. Le Marchand, L. R. Wilkens, P. Harwood, and R. V. Cooney.** Use of breath hydrogen and methane as markers of colonic fermentation in epidemiologic studies: circadian patterns of excretion ..... 199

**U. J. Nair, G. Obe, M. Friesen, M. T. Goldberg, and H. Bartsch.** Role of lime in the generation of reactive oxygen species from betel-quid ingredients ..... 203

**S. Tsugane, M. Tsuda, F. Gey, and S. Watanabe.** Cross-sectional study with multiple measurements of biologic markers for assessing stomach cancer risks at the population level ..... 207

**A. J. Likhachev, D. Sh. Beniashvili, V. J. Bykov, P. P. Dikun, M. L. Tyndyk, I. V. Savochkina, V. B. Yermilov, and M. A. Zabezhinski.** Biomarkers for individual susceptibility to carcinogenic agents: excretion and carcinogenic risk of benzo[*a*]pyrene metabolites ..... 211

**P. Keohavong and W. G. Thilly.** Determination of point mutational spectra of benzo[a]pyrene-diol epoxide in human cells ..... 215

## Contributed Articles

**J. Ashby and I. F. H. Purchase.** Commentary. Nongenotoxic carcinogens: an extension of the perspective provided by Perera ..... 223

**R. R. Watts, P. M. Lemieux, R. A. Grote, R. W. Lowans, R. W. Williams, L. R. Brooks, S. H. Warren, D. M. DeMarini, D. A. Bell, and J. Lewtas.** Development of source testing, analytical, and mutagenicity bioassay procedures for evaluating emissions from municipal and hospital waste combustors ..... 227

**J. R. Fowle, III and K. Sexton.** EPA priorities for biologic markers research in environmental health 235

**M. Y. Lichtveld, S. E. Rodenbeck, and J. A. Lybarger.** The findings of the Agency for Toxic Substances and Disease Registry Medical Waste Tracking Act Report ..... 243

**L. Thijs, J. Staessen, A. Amery, P. Bruaux, J.-P. Buchet, F. Claeys, P. De Plaen, G. Ducoffre, R. Lauwerys, P. Lijnen, L. Nick, A. Saint Remy, H. Roels, D. Rondia, and F. Sartor.** Determinants of serum zinc in a random population sample of four Belgian towns with different degrees of environmental exposure to cadmium ..... 251

**A. P. Watson and G. D. Griffin.** Toxicity of vesicant agents scheduled for destruction by the chemical stockpile disposal program ..... 259

### Meeting Report

**Y. Kurokawa and T. Damstra.** The Third United States–Japan Meeting on the Toxicological Characterization of Environmental Chemicals ..... 281

**Announcements** ..... 287

**Published Volumes of EHP** ..... 289

**Instructions to Authors** ..... 291